UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

EPA United States Environmental Protection Agency Office of Pesticide Programs

MEMORANDUM

3/28/2019

SUBJECT: Acute Toxicity Review for the use dilution (1: 254) of Liquid Pak Neutral Disinfectant Cleaner, EPA Reg. No.: 1839-176

FROM: Lindsay O'Dell
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THRU: Jenny Tao, Team Leader (Acute Toxicology)
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TO: Eric Miederhoff, PM Team 31 / Mohammad Alavi
Regulatory Management Branch I
Antimicrobials Division (7510P)

Registrant: Stephan Company		
Decision No.: 545766	Submission No.: 1026947	E-Sub No.: 33886
DP No.: 449895	Action Code: A570	
MRID No(s).: 50714801, 50714802, 50714803, 50714804, 50714805		

Formulation from label			
PC code(s)	CAS #(s)	Active Ingredient(s)	% weight
069105	68424-85-1	Alkyl (50% C14, 40% C12, 10% C16) dimethyl benzyl ammonium chloride	20.32%
069165	32426-11-2	Octyl decyl dimethyl ammonium chloride	15.24%
069166	5538-94-3	Dioctyl dimethyl ammonium chloride	7.62%
069149	7173-54-5	Didecyl dimethyl ammonium chloride	7.62%
		Other Ingredients	49.20%
		Total	100%

I. BACKGROUND

The Registrant, Stephan Company, has submitted an application to support a label amendment for their product: the use dilution (1: 254) of Liquid Pak Neutral Disinfectant Cleaner EPA Reg. No. 1839-176. The purpose of this label amendment is to prescribe precautionary statements for the secondary label of this end use product. The concentrated product is contained in water soluble packaging and diluted according to label directions to produce an end use solution.

II. FINDINGS/RECOMMENDATIONS

The five acute toxicity studies submitted for acute oral, acute dermal, acute inhalation, primary eye and skin irritation (MRID 50714801, -02, -03, -04, -05) were conducted on a dilution of EPA Reg. No. 1839-215. The subject product contains four active ingredients, whereas, the cited product contains two active ingredients. The concentrated form of both products are not substantially similar nor toxicologically relevant. Therefore, the formulations of both products post dilution were considered in order to make a bridging determination. The concentration of active ingredients in the diluted cited and diluted subject product are summarized below.

Cited product – use dilution 1839-215	**%**	**Subject product – use dilution 1839-176**	
Alkyl dimethyl benzyl ammonium chloride	0.186	Alkyl dimethyl benzyl ammonium chloride	0.0796
Didecyl dimethyl ammonium chloride	0.124	Didecyl dimethyl ammonium chloride	0.0299
		Dioctyl dimethyl ammonium chloride	0.0299
		Octyldecyl dimethyl ammonium chloride	0.0597

The certificate of analysis, provided by the Registrant indicates a total quaternary ammonium chloride concentration of 3100ppm (0.31%) for the cited product use dilution, EPA Reg. No. 1839-215. According to the use dilution directions of the subject product, EPA Reg. 1839-176, 0.1023 oz water soluble packet per 26 oz water (1:254) achieves a lower total quaternary ammonium chloride concentration than the cited product at 2000 ppm (0.2%). Additionally, when looking at the concentrations of individual active ingredients in the subject product compared to the cited product, the concentration of ADBAC and the total concentration of DDAC are both less than the cited product. Therefore, the data conducted on the cited product may be bridged to support the subject products secondary label precautionary statements.

1. Acute Oral Toxicity

An initial limit dose of 5000 mg/kg showed no mortality in 3 female rats, placing the product in Toxicity Category IV. MRID 50714801 is acceptable.

2. Acute Dermal Toxicity

The result of the 24-hour dermal exposure at a dose of 5000 mg/kg showed no mortality, placing the product in Toxicity Category IV. MRID 50714802 is acceptable.

3.Acute Inhalation Toxicity

The four-hour nose-only inhalation exposure resulted in a LC50 >2.33 mg/L in both males and females, placing the product in Toxicity Category IV. MRID 50714803 is acceptable.

4. Primary Eye Irritation

All evidence of irritation in three male rabbits cleared by 72 hours, placing the product in Toxicity Category III. MRID 50714804 is acceptable.

5. Primary Skin Irritation

All evidence of irritation in three male rabbits cleared by 24 hours, placing the product in Toxicity Category IV. MRID 50714805 is acceptable.

6. Dermal Sensitization

A dermal sensitization study was not submitted in this amendment. The concentrated product is a Nonsensitizer, thus, the diluted use solution is assigned the same classification.

7. The acute toxicity profile of the use dilution (1: 254) of Liquid Pak Neutral Disinfectant Cleaner, EPA Reg. No. 1839-176 is currently:

Study	MRID	Toxicity Category	Status
Acute Oral Toxicity	50714801	IV	Acceptable
Acute Dermal Toxicity	50714802	IV	Acceptable
Acute Inhalation Toxicity	50714803	IV	Acceptable
Primary Eye Irritation	50714804	III	Acceptable
Primary Skin Irritation	50714805	IV	Acceptable
Dermal Sensitization	-	Nonsensitizer	Assigned

III. CONCLUSION

The data submitted for the acute oral, acute dermal, acute inhalation, and primary eye and skin irritation endpoints is acceptable to support the label amendment for EPA Reg. No. 1839-176. In accordance with the Agency's Label Review Manual, the signal word "DANGER" must be reflected on the secondary label with the modified use dilution precautionary statements.

IV. PRODUCT LABELING – SECONDARY CONTAINER LABEL ONLY

1. Signal Word: DANGER

2. The statement, “Keep Out of Reach of Children (KOROC)”, is required. It should appear immediately above the front-panel signal word “DANGER”.

3. The Agency’s Label Review Manual, (https://www.epa.gov/sites/production/files/2017-09/documents/lrm-complete-aug-2017.pdf), suggests the following human-hazard precautionary statements:

HAZARDS TO HUMANS AND DOMESTIC ANIMALS:

> CAUTION: Causes moderate eye irritation. Avoid contact with eyes and clothing. Wear protective eye wear. Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, using tobacco or using the toilet. Remove and wash contaminated clothing before reuse.

FIRST AID:

> IF IN EYES: Hold eye open and rinse slowly and gently with water for 15-20 minutes. Remove contact lenses, if present, after the first 5 minutes, then continue rinsing. Call a poison control center or doctor for treatment advice.

DATA REVIEW FOR ACUTE ORAL TOXICITY TESTING (OCSPP 870.1100)

Product Manager: E. Miederhoff **Reviewer:** L. O'Dell

MRID No.: 50714801 **Study Completion Date:** 10/3/2011

Study No.: 11-028-3

Testing Laboratory: Tox Monitor Laboratories, Inc., Oak Park, IL.

Author: Michael Kukulinski

Quality Assurance (40 CFR §160): Included

Test Material: SC-RTU-3000

Dose levels: 5000 mg/kg bw

Animals: Rat, Sprague-Dawley

Number/Sex: 3 Females

Age: ~10 weeks

Weight: 244-278 grams

Source: Harlan Sprague Dawley, Indianapolis, IN

Method: OCSPP 870.1100; OECD 425

Summary:

1. **Estimated LD_{50}:** >5000 mg/kg bw
2. **Toxicity Category:** IV
3. **Classification:** Acceptable

Deviations from protocol: None.

Results:

An initial limit dose of 5,000 mg/kg was administered to one rat by oral gavage. Due to the absence of mortality in this rat, two additional rats received the same dose level. Since these animals survived, no additional animals were tested. No gross abnormalities were noted when the animals were necropsied at the conclusion of the 14-day observation period.

Table 1. Reported Mortality – Limit Test

Dosing Sequence	Dose Level (mg/kg bw)	Short-Term Outcome	Long-Term Outcome
1	5000	O	O
2	5000	O	O
3	5000	O	O

O = Survival; X = Death

DATA REVIEW FOR ACUTE DERMAL TOXICITY TESTING (OCSPP 870.1200)

Product Manager: E. Miederhoff **Reviewer:** L. O'Dell

MRID No.: 50714802 **Study Completion Date:** 9/29/2011

Study No.: 11-028-4

Testing Laboratory: Tox Monitor Laboratories, Inc., Oak Park, IL.

Author: Michael Kukulinski

Quality Assurance (40 CFR §160): Included

Test Material: SC-RTU-3000

Dose levels: 5000 mg/kg bw

Animals: Rabbit, New Zealand Albino

Number/Sex: 5 Males and 5 females

Age: At least 12 weeks

Weight: Males: 2600-2960 grams; Females: 2760 - 2950 grams

Source: Kuiper Rabbitry, Gary, Indiana

Summary:

1. **Estimated LD_{50}:** >5000 mg/kg bw
2. **Toxicity Category:** IV
3. **Classification:** Acceptable

Deviations from Guideline 870.1200:

None.

Results:

A 24-hour dermal exposure to the undiluted test material applied to previously clipped skin (about 10% of the total body surface area) at a nominal dose of 5000 mg/kg bw did not result in mortality during the

14-day observation period (Table 1). The animals all gained body weight during the study. Other than dermal irritation noted at the dose sites of all animals between Days 1 and 14, there were no other adverse clinical findings. No gross necropsy findings were observed.

Table 1. Mortality

Nominal dose (mg/kg bw)	Number Dead / Number Tested		
	Males	Females	Combined
5000	0 / 5	0 / 5	0 / 10

DATA REVIEW FOR ACUTE INHALATION TOXICITY TESTING (OCSPP 870.1300)

Product Manager: E. Miederhoff **Reviewer:** L. O'Dell

MRID No.: 50714803 **Study Completion Date:** 10/5/2011

Study No.: 11-028-6

Testing Laboratory: Tox Monitor Laboratories, Inc., Oak Park, IL.

Author: Michael Kukulinski

Quality Assurance (40 CFR §160): Included

Test Material: SC-RTU-3000

Concentrations: Chamber (gravimetrically determined): 2.33 mg/L

Nominal: 22.7 mg/L.

Chamber Type: Nose-only

Animals: Rat, Sprague-Dawley

Number/Sex: 5 males and 5 Females

Age: 8-12 weeks

Weight: Males: 203-217 grams; Females: 205 - 211 grams

Source: Harlan Sprague Dawley, Indianapolis, IN

Method: OCSPP 870.1300; OECD 403

Summary:

1. **LC_{50}:** Males: >2.33 mg/L

   Females: >2.33 mg/L
2. **Mean MMAD:** 2.67 µm (GSD = 3.36)
3. **Toxicity Category:** IV

4. **Classification:** Acceptable

Deviations from Guideline 870.1300: None.

Results:

The table below gives the mortality following a four-hour nose-only inhalation exposure to mean gravimetric concentrations of 2.33 mg/L of the undiluted test item as an aerosol.

At 2.33 mg/L, all animals survived exposure to the test atmosphere and gained body weight during the study. No clinical signs of toxicity were observed during the 14-day observation period. No gross abnormalities were noted for any of the animals when necropsied.

Reported Mortality

Exposure Concentration (mg/L)	Number dead / Number tested		
	Males	Females	Combined
2.33	0 / 5	0 / 5	0 / 10

Chamber Atmosphere

Mean (±SD) Exposure Conc. (mg/L)	Mean MMAD (µm)	Mean GSD	% of Particles < 3.3 µm
2.33 ± 0.18 (Range: 2.01-2.55)	2.67 (2.62, 2.72)	3.36 (3.21, 3.51)	56.9 (57.5, 56.2)

Chamber Environment

Exposure Level (mg/L)	2.33
Chamber Volume (L)	400
Total Airflow Rate (Lpm)	83
Temperature (°C)	19 - 21
Relative Humidity (%)	72 - 85

DATA REVIEW FOR ACUTE EYE IRRITATION TESTING (OCSPP 870.2400)

Product Manager: E. Miederhoff **Reviewer:** L. O'Dell

MRID No.: 50714804 **Study Completion Date:** 9/19/2011

Study No.: 11-028-1

Testing Laboratory: Tox Monitor Laboratories, Inc., Oak Park, IL.

Author: Michael Kukulinski

Quality Assurance (40 CFR §160): Included

Test Material: SC-RTU-3000

Dose levels: 0.1 mL

Animals: Rabbit, New Zealand Albino

Sex: 3 Males

Age: 10-12 weeks

Weight: 2920-3250g

Source: Kuiper Rabbitry, Gary, Indiana

Summary:

1. **Toxicity Category**: III
2. **Classification**: Acceptable

Deviations from Guideline 870.2400 and other comments: None.

Results:

The tables below provide the results ("positive" irritation and mean total irritation scores) following instillation of 0.1 mL of the undiluted test material into one eye of three rabbits. All animals gained body

weight during the study. Apart from the eye irritation noted below, there were no other signs of toxicity. There were some eye irritation reactions in all of the test subjects and the maximum group mean score was 8.66/110.0 at the 1 hour observation. All irritation cleared by the 72-hour observation and the study was terminated.

Incidence of Irritation

Time Post-Instillation	No. of Animals Testing "Positive" / No. of Animals Tested			
	Corneal Opacity	Iritis	Conjunctiva [a]	
			Redness	Chemosis
1 hour	0 / 3	0 / 3	0 / 3	0 / 3
24 hours	0 / 3	0 / 3	1 / 3	0 / 3
48 hours	0 / 3	0 / 3	0 / 3	0 / 3
72 hours	0 / 3	0 / 3	0 / 3	0 / 3

[a] Redness or chemosis score of 1 not considered a "positive score" according to EPA 870.2400.

Severity of Irritation

Time Post Instillation	Mean Total Score [a]
1 hour	8.66
24 hours	7.66
48 hours	4.66
72 hours	0.0

[a] Draize method of scoring (1944).

DATA REVIEW FOR ACUTE DERMAL IRRITATION TESTING (OCSPP 870.2500)

Product Manager: E. Miederhoff **Reviewer:** L. O'Dell

MRID No.: 50714805 **Study Completion Date:** 9/19/2011

Study No.: 11-028-2

Testing Laboratory: Tox Monitor Laboratories, Inc., Oak Park, IL.

Author: Michael Kukulinski

Quality Assurance (40 CFR §160): Included

Test Material: SC-RTU-3000

Dose levels: 0.5 mL

Animals: Rabbit, New Zealand Albino

Number/Sex: 3 Males

Age: 10-12 weeks

Weight: Males: 2750-2980 grams

Source: Kuiper Rabbitry, Gary, Indiana

Summary:

1. **Toxicity Category:** IV
2. **Classification:** Acceptable

Deviations from Guideline 870.2500: None.

Results:

The table below provides the individual Draize scores from four-hour dermal exposures of three male rabbits to 0.5 mL of the undiluted test material applied to intact clipped application sites measuring 6

cm^2. The primary skin irritation index (PDII) was calculated to be 0.42. Minimal irritation reactions were observed in all of the test subjects which cleared by the 24 hour observation. The test material was slightly irritating (US EPA, 1988).

Individual Dermal Irritation Scores following the four-hour exposure

Animal No.	Sex	Erythema / Edema			
		Time After Patch Removal			
		60 minutes	24 hours	48 hours	72 hours
595	M	1 / 0	0 / 0	0 / 0	0 / 0
596	M	1 / 1	0 / 0	0 / 0	0 / 0
597	M	1 / 1	0 / 0	0 / 0	0 / 0